--106. (New) The method of claim 103, wherein the cancer is of epithelial origin.--

--107. (New) The method of claim 103, wherein the cancer is of neuroectodermal origin.--

--108. (New) The method of claim 107, wherein the cancer of neuroectodermal origin is a melanoma.--

REMARKS

Claims 57-101 were pending in the subject application. Applicants have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108. Support for these claims may be found inter alia in the specification as follows: claims 102-103: page 11, line 13 to page 12, line 2; page 76, lines 19-21; page 30, line 9; page 12, lines 15-16; page 15, lines 11-22; page 15, line 26 to page 16, line 20; claims 104-105: page 18, lines 5-10; claims 106-108: page 17, lines 5-10. Claims 102-108 do not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested.

Composition claims

The Examiner stated that the previously submitted composition claims 57-70 and newly submitted claims 98-101 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the compositions as claimed are distinct because they can be used in a materially different process such as linked to a column for purification of cross reactive antibodies, in an in vitro method to study immune responses or in an in vitro method to generate monoclonal antibodies. The Examiner stated that since applicant has received

an action on the merits for the originally presented methods invention, this invention has been constructively elected by original presentation for prosecution on the merits and accordingly, claims 57-70 are withdrawn from consideration as being directed to a non-elected invention. The Examiner stated that applicants assert that the claims do not define patentably distinct inventions and the groups should be rejoined. Applicants remarks are not persuasive because the compositions can be used in materially different methods and are distinct as set forth above, the restriction is proper and made final. The Examiner stated that the inventions are related as disclosed but distinct as claimed, and restriction is proper. The Examiner stated that there is no requirement that the invention be both independent and distinct as asserted by applicants, and cited MPEP 803 "the inventions must be independent or distinct as claimed." The Examiner moreover stated that there is an undue search and examination burden since the inventions are classified differently necessitating a different search of at least the US Patents. The Examiner further stated applicants may not petition under 37 CFR 1.29(b) to rejoin because no restriction has been made in the present application due to actions by the applicant, as clearly evidenced by the cancellation of compositions in preliminary amendments A mailed June 7, 1995 and B, mailed November 15, 1995.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108. Applicants respectfully point out that newly added claims 102-108 are all method claims, not composition claims. Applicants contend that this amendment obviates the above rejection and respectfully request that the Examiner reconsider and withdraw this

ground of rejection.

Priority

The Examiner stated that applicants recently filed a request for a corrected filing receipt indicating that the instant application was a 371. The examiner stated that the instant application was not filed under 35 USC 371 and that it is not now nor ever has been accorded 371 status. The Examiner that correction is required in response to this office action.

In response, applicants will file a request for a corrected filing receipt to obviate the Examiner's above objection.

Obviousness type double patenting

The Examiner provisionally rejected claims 71-97 under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 65-71 and 77 of copending Application No. 08/477,097. The Examiner stated although the conflicting claims are not identical, they are not patentably distinct from each other because they all claim conjugating proteins to gangliosides through the ceramide portion and thus the particular method species drawn to GM2 or GM3 claimed in the copending application would anticipate the instant genus method claims. The Examiner stated applicants' argue that the provisional rejection should be allowed to drop and that the instant claims be allowed to issue, pursuant to MPEP section 804. The Examiner stated since the instant claims are not allowable, the provisional double patenting rejection is maintained for reasons already made of record.

The Examiner provisionally rejected claims 71-97 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 66-72 of copending Application No. 08/475,784. The Examiner stated although the conflicting claims are not identical, they are not patentably distinct from each other because they all claim conjugating proteins to gangliosides through the ceramide portion and thus the particular method species claimed in the copending application would anticipate the instant genus method claims. The Examiner stated applicants' argue that the provisional rejection should be allowed to drop and that the instant claims be allowed to issue, pursuant to MPEP section 804. The Examiner stated since the instant claims are not allowable, the provisional double patenting rejection is maintained for reasons already made of record.

The Examiner provisionally rejected claims 71-97 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 80-86 and 92-96 of copending Application No. 08/196,154. The Examiner stated although the conflicting claims are not identical, they are not patentably distinct from each other because they all claim conjugating proteins to gangliosides through the ceramide portion and thus the particular method species claimed in the copending application would anticipate the instant genus method claims. The Examiner stated applicants argue that the provisional rejection should be allowed to drop and that the instant claims be allowed to issue, pursuant to MPEP section 804. The Examiner stated since the instant claims are not allowable, the provisional double patenting rejection is maintained for reasons already made of record.

In response, applicants without conceding the correctness of the above rejection but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without disclaimer or prejudice to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108. Newly submitted claim 102 recites as follows: "A method of stimulating or enhancing antibody production in a subject which comprises administering to the subject an effective amount of a composition which comprises: a) a conjugate of i) an oligosaccharide to ii) Keyhole Limpet Hemocyanin; b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and c) a pharmaceutically acceptable carrier; the relative amounts of such conjugate and such saponin being effective to stimulate or enhance antibody production in the subject, so as to thereby stimulate or enhance antibody production in the subject." In contrast, the claims of the copending applications do not recite the word "oligosaccharide." These copending applications further recite that the conjugation is through the ceramide portion of the ganglioside derivative. The conjugation in the claims of the subject application are not through a ceramide portion since an oligosaccharide does not contain a ceramide portion. Therefore, the subject claims are not an obvious variation of the inventions claimed in the copending applications. Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 71-97 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained for reasons made of

record for claims 44 and 46-56 in Paper No. 13, mailed 4-1-98 and reasons herein. The Examiner stated as to claims 72-77 and 89-97, Applicants arguments and evidence have been carefully evaluated but is not persuasive to remove the rejections of record in regard to prevention of cancer, and prevention of relapse of cancer. The Examiner stated that applicants provide Zhong et al (Cancer Research, 58:2844-2849, 1998) and contend that Zhong et al protects against syngeneic tumor challenge and eliminates micro metastases. The Examiner stated this evidence is not persuasive for instant prevention of cancer or prevention of relapse for the reasons set forth below. The Examiner stated first, the composition did not prevent cancer as is claimed (see claims 72 and dependent claims). The Examiner stated as seen on page 2846, while the composition comprising GD2 conjugated to KLH via the ceramide double bond to aldehyde by ozonolysis and attachment of KLH by reductive amination in the presence of cyanoborohydride in combination with QS-21 extended survival, however, mice still died. The Examiner stated prevention of cancer is not still enabled even with the composition comprising GD2 conjugated to KLH via the ceramide double bond to aldehyde by ozonolysis and attachment of KLH by reductive amination in the presence of cyanoborohydride in combination with QS-21. The Examiner stated in regard to prevention, the tumor challenge was limited to a single type of cancer and administered by intravenous challenge. The Examiner stated the claims are broadly drawn to prevention of any cancer and is not limited to the specific conjugate and lymphoma treated. The Examiner stated in contrast to solid tumors, the intravenous compartment would be expected to have any antibodies present in high concentration. The Examiner stated this situation is unlike the majority of cancers which are not present in the intravenous compartment. The Examiner stated

applicants have not provided evidence that solid tumors can be either treated or prevented by administration of any compositions as is claimed. The Examiner stated Curti et al (Critical Reviews in Oncology/Hematology, 14:29-39, 1993) teach the numerous physical barriers to drug delivery in solid tumors. The Examiner stated applicants have not taught these types of cancers can be prevented prior to the onset of cancer or any relapse also prevented. The Examiner stated Zhong et al teach that the administration of the composition after a reduced tumor challenge did not provide a statistically significant difference (see page 2847, column 1, second full paragraph) between the control and the composition. The Examiner stated thus, prevention is not enabled and relapses are not enabled since the Zhong et al article does not enable prevention of relapse, because the primary tumor is still present and relapse can occur at the primary tumor site. The Examiner stated all relapses are not due to metastacies. The Examiner stated thus, the specification as originally filed does not enable the prevention of any type of cancer.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108. Applicants respectfully point out that new claim 102 recites a "method of stimulating or enhancing antibody production in a subject" and new claim 103 recites "a method of treating a cancer in a subject." Applicants contend that these amendments obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Claims 71-97

The Examiner stated that as to claims 71-97, the claims are still not enabled for derivatives of KLH wherein the derivative is comprises KLH linked to an immunological adjuvant. The Examiner stated the specification does not teach how to link or conjugate immunological adjuvants, such as cytokines, non-ionic block copolymer or monophospholipid A, to the KLH moiety. The Examiner stated the specification does not teach that the compositions so made function to boost the immune response toward the oligosaccharide moiety, rather than the KLH moiety to which the adjuvant is attached or are useful in any manner contemplated by the specification. The Examiner stated the specification does not reference any art accepted method of making said derivatives. The Examiner stated Pierce (U.S. Patent No. 5,616,477) teaches that many materials have been shown to have adjuvant activity, however, such chemical coupling involves harsh treatment and often results in destruction of a portion of the antigen and reduced immunogenicity (column 1, lines 30-40). The Examiner stated applicants have not taught how to make a ganglioside or oligosaccharide portion of the ganglioside retains its immunogenicity at any level, especially at that level which is required to treat or prevent cancer as is instantly claimed. The Examiner stated moreover, the art teaches that the antigen *per se* is directly coupled to the immunological adjuvant. The Examiner stated the claim requires that the adjuvant be linked through the KLH carrier protein and thus the adjuvant would be expected to increase the immunogenicity of the KLH rather than the ganglioside or oligosaccharide attached thereto. The Examiner stated in view of the absence of showing of the ability of such compositions to prevent of cancer or prevent relapses of cancer, the absence of any

teaching of how to make these derivatives suitable for use in the claimed methods, one skilled in the art would be forced into undue experimentation to make such derivatives and use them in the methods of the invention as are now claimed. The Examiner stated in the absence of further guidance on how to make a ganglioside-KLH derivative, it would require undue experimentation to predictably and reproducibly make the compositions and use the compositions in the claimed.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108 which do not recite "derivatives of Keyhole Limpet Hemocyanin." Applicants contend that these amendments obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 71-88 under 35 U.S.C. 103(a) as being unpatentable over Livingston et al (Cancer Research, 49:7045-7050, 1989) in view of Irie et al (U.S. Patent No. 4,557,931, published December 10, 1985) and Ritter et al (Cancer Biology, 2:401-409, 1991) is maintained and reiterated below. The Examiner stated that Livingston et al (Cancer Research, 49:7045-7050, 1989) teach a composition administered to melanoma patients for stimulating the production of antibodies directed to a carbohydrate epitope on the ganglioside, GM2 (p 7046-7048). The Examiner stated Livingston et al teach that the GM2 is administered in conjunction with an

adjuvant, Bacillus Calmette-Geurin (BCG), and a pharmaceutically acceptable vehicle, phosphate buffered saline (p 7048, column 1, paragraph 3 and paragraph bridging p 7046-47). The Examiner stated Livingston et al teach that the melanoma recurrence was delayed in patients developing GM2 antibodies after vaccination (p 7048, paragraph 1 and column 2, paragraph 2). The Examiner stated Livingston et al teach that more patents produced IgM antibodies that IgG antibodies to the GM2 (9 7047 paragraph bridging columns 1-2). The Examiner stated Livingston et al also teach the gangliosides GM2, GD2 and GD3 are expressed on the cell surface of human malignant melanomas (p 7045, column 1, paragraph 2). The Examiner stated Livingston et al do not teach the conjugation of the GM2 vaccine with Keyhole Limpet Hemocyanin (KLH) through the ceramide portion of the ganglioside or use of any of the other gangliosides in a method to induce an immune response or cancer treatment.

The Examiner stated that Irie et al teach conjugation of ganglioside GM2 to a non-toxic protein carrier, such as albumin, using ozonolysis (column 5, see B., lines 19-68) which conjugates a the GM2 through the ceramide portion. The Examiner stated Irie et al teach that the fatty acid of ceramide maybe removed leaving shpingosine and thus the coupling takes place through the amine group of the sphingosine moiety (column 2, lines 64-69). The Examiner stated Irie et al teach that the conjugated GM2 can be used as a vaccine to stimulate an immune response and raise the anti-GM2 titer in mammals (column 2). The Examiner stated Irie et al differ by not conjugating the GM2 to KLH.

The Examiner stated that Ritter et al (Cancer Biology, 2:401-409,

1991) teach that the IgG responses to gangliosides may be increased by the covalent attachment of foreign carrier proteins such as KLH to the gangliosides resulting in the T cell help necessary for the response (p 406, paragraph 1). The Examiner stated Ritter et al discloses the advantage of using an IgG antibody response (versus IgM) against ganglioside is that IgG a) has a higher affinity; b) is better able to penetrate solid tissues; c) is able to mediated antibody-dependent cell-mediated cytotoxicity; and d) is generally detectable in the serum for longer periods after immunization. The Examiner stated it would have been *prima facie* obvious to one of ordinary skill in the art to modify the GM2-albumin ceramide conjugate of Irie et al by substituting KLH for albumin and to substitute the resulting GM2-KLH ceramide conjugate for the GM2 in the immunization composition of Livingston et al for active immunization for generating antibody response for melanoma treatment because Irie et al teach that the GM2 conjugated through the ceramide (sphingosine) portion can be used as a vaccine to simulate an immune response and raise the anti-GM2 titer in mammals and Ritter et al teach that the IgG responses to gangliosides may be increased by covalent attachment of foreign carrier proteins such as KLH to the gangliosides resulting in the T cell help necessary for the response (p 406, paragraph 1) and Ritter et al discloses the advantages of generating and IgG as opposed to an IgM antibody response and optimization of the dosage, route of administration and number of sites to administer the composition as combined above is well within the skill of the art.

The Examiner stated applicants allege that the references neither individually or combined teach the invention as is now claimed. The Examiner stated this is not persuasive. The Examiner stated

applicant's arguments fail to comply with 37 CFR. 1.111(b) because they amount to a general allegation that the claims patentably distinguishes them from the references. Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. The Examiner stated further, they do not show how the amendments avoid such references or objections.

The Examiner rejected claims 71-88 under 35 U.S.C. 103(a) as being unpatentable over Livingston et al. (Cancer Research, 149:7045-7050, 1989) in view of Ritter et al. (Seminars in Cancer Biology, 2:401-409, 1991), Liane et al (Journal of Biological Chemistry, 249(14):4460-4466, 1974), Livingston et al. (U.S. Patent No. 5,102,663), Ritter et al. (Immunobiol, 182:32-43, 1990), Kensil et al. (The Journal of Immunology, 146(2):431-437, 1991), and Marciani et al. (Vaccine, 9:89-96, 1991) and Uemura et al (J Biochem, 79(6):1253-1261, 1976). The Examiner stated that Livingston et al (Cancer Research) teach a composition administered to melanoma patients for stimulation the production of antibodies directed against a carbohydrate epitope on the ganglioside, GM2 (page 7046-7048). The Examiner stated Livingston et al teach that the composition for treatment is administered at a concentrations of 100,200, or 300 ug with an adjuvant, Bacillus-Calmette-Geurin (BCG), and a pharmaceutically acceptable vehicle, phosphate buffered saline (p 7046, column 1, paragraph 3, and paragraph bridging p 7046-47). The Examiner stated Livingston et al teach that melanoma recurrence was delayed in patients developing GM2 antibodies after treatment with the composition (page 7048, paragraph 1 and column 2, paragraph 2). The Examiner stated

Livingston et al teach that more patients produced IgM antibodies than IgG antibodies to the GM2, GD2 and GD3 are expressed on the cell surface of human malignant melanomas (page 7045, column 1, paragraph 2). The Examiner stated Livingston et al teach treatment of a melanoma, a cancer which is both epithelial and neuroectodermal in origin. The Examiner stated Livingston et al differ by not teaching the conjugation of the GM2 or other gangliosides by means of a carbon on the ceramide moiety with aminolysyl groups on Keyhole Limpet Hemocyanin (KLH) in a composition and using this composition for treatment. The Examiner stated that Ritter et al (1991) teach that IgG responses to gangliosides may be increased by the covalent attachment of foreign carrier proteins such as KLH to the gangliosides resulting in the T cell help necessary for the response (page 406, paragraph 1). The Examiner stated Ritter et al teaches discloses that the advantage of inducing an IgG antibody response (vs IgM) against gangliosides is that IgG: a) has a higher affinity, b) is better able to penetrate solid tissues, c) is able to mediate antibody-dependent cell-mediated cytotoxicity, d) and is generally detectable in the serum for longer periods after immunization. The Examiner stated Liane et al (Journal of Biological Chemistry, 249(14):4460-4466, 1974) teach a method for covalent coupling of gangliosides to aminoethyl agarose or the amino group bearing glass beads by oxidative ozonolysis of the olefinic bond of the shpingosine moiety (i.e. the instant carbon double bond of ceramide) and coupling of the carboxyl bearing product to the amino group of aminoethyl agarose or the amino group bearing glass beads. The Examiner stated Ritter et al (1990) teach that GD3 lactone is more immunogenic than GD3. The Examiner stated Livingston et al (U.S. Patent No. 5,102,663) teach that gangliosides GM3, GM2, GD3,

GD2, GT3 and O-acetyl GD3 are gangliosides that are prominent cell-membrane components of melanoma and other tumors of neuroectodermal origin (column 1, lines 22-28). The Examiner stated Kensil et al teach that QS-21 (i.e. the instant carbohydrate derivable from the bark of the Suillaja saponaria Molina tree) produced a higher antibody response than conventional aluminum hydroxide (page 433, column 2, paragraph 4 and Figure 3). The Examiner stated Kensil et al also teach that the immune responses obtained with QS-21, reached a plateau at doses between 10-80 ug in mice (page 433, column 1, paragraph 3). The Examiner stated Maricani et al teach the use of QS-21 adjuvant was useful because it did not cause a toxic reaction in cats (page 93, paragraph 1). The Examiner stated Uemura et al (J Biochem, 79(6):1253-1261,1976) teach that the ozonolysis and reduction of various sphingolipids did not affect the haptenic reactivity of the ganglioside derivative with antibodies. The Examiner stated it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the composition taught by Livingston et al by conjugating the GM2 to KLH by covalently coupling GM2 to KLH by substituting GM2 for the globoside and KLH for the aminoethyl agarose to produce a GM-2-KLH conjugate by means of the olefinic bond of the sphingosine moiety of the GM2 (i.e. the instant ceramide double bond) and the e-aminolysyl groups present in the KLH protein using the method of Liane et al and add QS-21 as an adjuvant to the GM-2-KLH conjugate for use as a vaccine because the conjugated composition would be expected to enhance the IgG response to the ganglioside, as taught by Ritter et al (1991), thus providing the advantages by Ritter et al (1991) and adding the QS-21 would be advantageous because it provides for a higher antibody response that the commonly used adjuvant use by Kensil et al and

QS-21 provides the advantages that is not toxic to animals as is taught by Marciani et al. The Examiner stated it also would have been *prima facie* obvious to use doses of between 10 and 80 ug of QS-21 in the composition and optimize the dose accordingly because the immune response with QS-21 plateaus at doses between 10-80 ug and optimization of the weight of ratio of the components of the composition to provide an optimal response is well within the ordinary skill in the art and use the composition as modified supra for treatment of melanoma as taught by Livingston et al (Cancer Research). The Examiner stated it would have been *prima facie* obvious to one of ordinary skill in the art to substitute any one of GM3, GD2, GD3, or O-acetyl GD3 for the GM2 ganglioside in the composition and method as combined supra because they are all prominent cell-membrane components of melanomas as taught by Livingston et al (U.S. Patent No. 5,102,663) and one of ordinary skill in the art at the time the invention was made to substitute the GD3 lactone for the GM2 ganglioside in the composition because GD3 lactone is more immunogenic than GD3, as taught by Ritter et al (1990) and would be expected to product an enhanced antibody response as compared to GD3. The Examiner stated Optimization of the dosage, route to immunization, number of sites of immunization to administer the composition is will within the skill of the ordinary artisan. The Examiner stated one would have reasonably expected the conjugation procedure to work as substituted because conjugation through the ε-aminolysyl groups of carrier proteins for enhance immunogenicity is routine in the art and Uemura et al (J Biochem, 79(6)1253-1261, 1976) teach that the ozonolysis and reduction of various sphingolipids did not affect the haptenic reactivity with antibodies.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-18. New claim 102 recites a "method of stimulating or enhancing antibody production in a subject which comprises administering to the subject an effective amount of a composition which comprises: a) a conjugate of i) an oligosaccharide to ii) Keyhole Limpet Hemocyanin; b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and c) a pharmaceutically acceptable carrier; the relative amounts of such conjugate and such saponin being effective to stimulate or enhance antibody production in the subject, so as to thereby stimulate or enhance antibody production in the subject." New claim 103 recites a "method of treating a cancer in a subject which comprises administering to the subject an effective cancer preventing or treating amount of a composition which comprises: a) a conjugate of i) an oligosaccharide to ii) Keyhole Limpet Hemocyanin; b) a saponin derivable from the bark of a Quillaja saponaria Molina tree; and c) a pharmaceutically acceptable carrier; the relative amounts of such conjugate and such saponin being effective to stimulate or enhance antibody production in the subject, so as to thereby prevent or treat a cancer in a subject." None of the cited references teach, suggest or disclose applicants' claimed invention. Applicants contend that these amendments obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 71-97 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner stated this is a new matter rejection. The Examiner stated as to claims 71-97, Applicants point to page 32, lines 1-33 and page 12, lines 4-14 for support for the now claimed invention. The Examiner stated this is not persuasive, the passage at page 32, lines 4-14 provide for a specific coupling procedure at the C-4 carbon of the sphingosine moiety of the ceramide to the ε-aminolysyl group of a proteins (ozonolysis, production of a functional aldehyde group and coupling to an ε-aminolysyl group on a protein by reductive amination). The Examiner stated the passage at page 12, lines 4-14 in combination with the passage at page 32, lines 1-33 does not support a broad coupling to any generic portion of the ceramide backbone of the ganglioside, by any generic means by cleavage of any double bond (i.e. C=O) and coupling by any linkage process. The Examiner stated the written description at pages 12 and 32 does not support by way of written description, convey that applicants had at the time of filing contemplated any means of coupling to any not in possession of that which is now broadly claimed. The Examiner stated correction is required.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108. Applicants contend that this amendment obviates the above rejection and respectfully request that the examiner reconsider and withdraw this ground of rejection.

The Examiner stated as to claims 89-97, the concept of using the composition for preventing a relapse of cancer in a subject comprising administering the composition is not found in either the detailed description of the invention at pages 11-18, nor at the indicated pages of 12,32,33,76,114 or 116 of the specification as alleged by applicants. The Examiner stated the issue is best resolved by applicants pointing to the specification by page and line number where written description support for conception of this now claimed invention can be found.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have hereinabove canceled claims 57-101 without prejudice or disclaimer to their right to pursue the subject matter of these claims in a later-filed application and added new claims 102-108. Applicants contend that this amendment obviates the above rejection and respectfully request that the examiner reconsider and withdraw this ground of rejection.

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 102-108.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $580.00 fee which includes the $445.00 fee for a three-month extension of time and the $135.00 fee for additional claims, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

10/11/00
John P. White Date
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